BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,265	11/28/2001	James F. Young	10271-048	3847

20583 7590 08/12/2003

PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER	
CHEN BROWN, STACY	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 08/12/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/996,265	YOUNG ET AL.	
	Examiner	Art Unit	
	Stacy B Chen	1648	

-- The MAILING DATE of this communicati n appears n the cover sheet with the corresp ndenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-127* is/are pending in the application.

4a) Of the above claim(s) *41-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-40 and 53-127* is/are rejected.

7)☒ Claim(s) *1 and 28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election of Group I, claims 1-40 and 53-127 is acknowledged. Claims 1-127 are pending. Claims 41-52 are withdrawn from consideration, being drawn to non-elected subject matter. Applicant mainly traverses that the restriction requirement for the election of one antibody construct should be a species election. The examination of all the sequences would be a tremendous burden on the Office and therefore the restriction requirement is deemed proper and made FINAL. If the elected sequences are found to be free of the prior art, all appropriate claims containing the allowable sequence will be rejoined.

Claim Objections

2. Claims 1 and 28 are objected to because of the following informalities: Claim 1, line 1, there should be a comma following "preventing". Claim 28, line 33, after "administration", there should be an "of".

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-40 and 53-127 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "effective amount" of antibodies or fragments thereof. The claims should indicate the metes and bounds of "effective" so that one of skill in the art would know when effective treatment has occurred.

Claims 66-73, 90-95, 101, 105, 122-127 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 66-73, 90-95, 101, 105, 122-127 contain the trademark/trade name SYNAGIS®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe palivizumab and, accordingly, the identification/description is indefinite.

Claims 86-89 and 93-111, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims lack comparative basis for "increased *in vivo* half-lives". To what standard is "increased" measured against? Clarification is required.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-11, 13-18, 21, 23-26, 28-34 and 36-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Subramanian *et al* (*Ped. Infect. Dis. J.* 1998, 17:110-115). The claims are drawn to a method of preventing, treating or ameliorating one or more symptoms associated with RSV infection in a mammal comprising administering one or more antibodies or fragments thereof that immunospecifically bind to the one or more RSV antigens, administered in the amount of 15 mg/kg. The antibodies are humanized, monoclonal antibodies. A dosage of less than 15 mg/kg results in a serum titer of antibodies less than 30 micrograms/ml at least 20 days after the first dose and prior to the subsequent dose.

Subramanian teaches the administration of palivizumab (also called Medi-493 and SYNAGIS®) to infants, administered intravenously at 3, 10 and 15 mg/kg (page 110) once a month, for up to five doses. Their antibody had a mean half-life of 20 days. The serum concentrations after 30 days were 6.8 micrograms/ml in those subjects having received a 3 mg/kg dose of antibodies (page 110, column 2).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 53-84, 86-110, 112-120 and 122-127 are rejected under 35 U.S.C. 103(a) as being unpatentable over MedImmune, Inc. (SYNAGIS® package insert) or Subramanian *et al* (*Ped.*

Infect. Dis. J. 1998, 17:110-115) in view of Lam *et al* (*Proc. Int'l Symp. Rel. Bioact. Mater.*, 1997, 24:759-760) in view of Gonzalez *et al* (6,117,980).

The claims are drawn to methods of using sustained release formulations of antibodies that bind to RSV, in order to prevent, treat or ameliorate one or more symptoms of RSV infection in a mammal. The antibodies can be SYNAGIS® palivizumab or HL-SYNAGIS®. The dosage of antibodies is approximately 15 mg/kg or less, and is administered via different routes, including intravenous, intramuscular and pulmonary routes.

MedImmune and Subramanian teach the administration of palivizumab (also called Medi-493 and SYNAGIS®) to infants. MedImmune administers the antibody at 15 mg/kg (see insert) and Subramanian administers the antibody intravenously at 3, 10 and 15 mg/kg (page 110). MedImmune's package insert for SYNAGIS™ discloses increased half-lives of an *average* 20 days administered to pediatric patients less than two years old. The concentrations of antibodies achieved with intramuscular injections of 15 mg/kg resulted in concentrations of 37 +/- 21 μg/ml (16 to 58 μg/ml) after the first injection, see column 1, "Clinical Pharmacology". The dosage recommended is 15 mg/kg of body weight, on a monthly basis during RSV season (November through April). MedImmune and Subramanian fail to teach a sustained release formulation and pulmonary administration of the antibody.

However, Lam *et al* (*Proc. Int'l. Symp. Control Rel. Bioact. Mater.*, 1976, 24:759-760) discloses sustained release microencapsulation pharmaceutical formulations of recombinant humanized monoclonal antibodies for patients with macular degeneration, see abstract.

Further, Gonzalez teaches the administration of a humanized anti-IL-8 monoclonal antibody or fragments thereof via known therapeutic formulation methods, such as inhalation,

injection, intramuscular and sustained release. The antibody is administered systemically or at a site of inflammation (col. 60, lines 53-60).

It would have obvious to administer a sustained release formulation of palivizumab via inhalation. One would have been motivated to use a method of inhalation to administer to the lungs because Gonzalez teaches known methods of preparing humanized antibodies or fragments thereof for inhalation. Lam teaches the preparation of a sustained release formulation comprising humanized monoclonal antibodies, suggested by Gonzalez for administration. Given that the lungs are primarily affected by RSV infection, one would have been motivated to administer palivizumab closer to the site of infection, as suggested by Gonzalez (col. 60, lines 59-60). One would have had a reasonable expectation of success that the palivizumab would work in a therapeutic formulation for inhalation because Gonzalez administers a humanized antibody and fragments thereof by inhalation. With regard to the specific amounts of palivizumab in the body after 20 days, one of ordinary skill in the art would have been able to optimize the sustained release formulation to maintain the necessary concentration of antibody for effective therapy.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 53-65 are provisionally rejected under the judicially created doctrine of double patenting over claims 85-191 of copending Application No. 09/724,396. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: methods of preventing, treating or ameliorating one or more symptoms associated with an RSV infection comprising administering antibodies that immunospecifically bind to an RSV antigen, wherein the antibodies are in a sustained release composition.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Conclusion

7. No claim is allowed. The antibody claimed in claims 12, 27, 40, 85, 111 and 121, A4B4-L1FR-S28R, is free of the prior art. A4B4-L1FR-S28R does not have the benefit of the filing date of the parent application, USSN 09/724,396.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 located in Crystal Mall 1. The Fax number for Art Unit 1648 is (703) 308-4426. All Group 1600 Fax machines will be available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stacy B. Chen, whose telephone number is (703) 308-2361. The Examiner can normally be reached on Monday through Friday from 7:30 AM-4:00 PM, (EST). If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, James C. Housel, can be reached at (703) 308-4027. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SBC

Stacy B. Chen
August 5, 2003

James C. Housel 8/8/03
JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600